

## Amendments To The Claims

### Claims

1. [Cancelled]

2. [Cancelled]

3. [Cancelled]

4. [Currently Amended] A method for ~~obtaining signature probes comprising the steps of:~~  
~~Compiling a database of nucleic acid sequences from a substantially homologous region of an RNA or~~  
~~DNA comprising sequences from all organisms or viruses that will be incorporated into the analysis;~~  
~~Compiling a bifurcating tree that shows the genetic relationships between the organisms whose nucleic acid~~  
~~sequences will be included in the analysis;~~  
~~Calculating the occurrence frequency and distribution of every oligoribonucleotide or~~  
~~oligodeoxyribonucleotide sequence of length N in the sequence database;~~  
~~Calculating a signature quality function which measures the extent to which each particular~~  
~~oligoribonucleotide or oligodeoxyribonucleotide sequence of length N is characteristic of each node in a~~  
~~substantially bifurcating substantially phylogenetic tree of genetic relationships;~~  
~~Selecting a oligoribonucleotide or oligodeoxyribonucleotide sequence as a signature for a particular node if~~  
~~the quality index for said sequence has its greatest value for that node and the quality index exceeds a~~  
~~preset value;~~  
~~Synthesizing signature probes appropriate for use in a hybridization experiment that incorporate the node-~~  
~~specific information of the signature sequences.~~

determining the genetic affinity of organisms or viruses in a test sample  
containing a nucleic acid comprising the steps of:

A. Obtaining or developing a bifurcating node phylogenetic tree that  
substantially reflects the genetic relationship between the organisms or  
viruses included in a database of sequences of the nucleic acid.

B. Identifying the extent to which each particular oligonucleotide or  
sequence of length N is characteristic of each node in the bifurcating  
node phylogenetic tree of genetic relationship

C. Deriving a plurality of nucleic acid signature probes from a signature-  
database of signature sequences that are complementary to a portion of

the nucleic acid sequence of the organism or virus such that the number of organisms or viruses whose genetic affinity might be determined is at least twice the number of probes used.

D. Hybridizing the signature probes to the nucleic acid obtained from the test sample under conditions where a detectable signal will be produced by signature probes that hybridize to the nucleic acid of the organism or virus.

E. Identifying signature probes which produce detectable signal;

F. Determining which nodes in the bifurcating node phylogenetic tree of genetic relationship produced detectable signal to identify the closest genetic relatives of the organism or virus in the test sample.

5. [Currently Amended] A method of claim 4 wherein the signature probes are comprised of a moiety selected from the group consisting of: RNA, DNA, an analog of RNA or DNA including peptide nucleic acids, 2-O-methyl DNA or any other molecule that can interact with the test sample nucleic acid in a sequence-specific way.

6. [Currently Amended] A method of claim 4 wherein the hybridization step utilizes a feature selected from the group consisting of an immobilized array of signature probes, molecular beacons and a hybridization step done in solution.

7. [Previously Presented] A method of claim 4 wherein the detection step utilizes radioactive labels, chemiluminescence and/or fluorescence.

8. [Currently Amended] A method of claim 4 wherein ~~a tree of relationships signifying the bifurcating node phylogenetic tree of genetic relationships signifying genetic relationship~~ is generated by a standard method selected from the group consisting of parsimony method, distance method, and maximum likelihood.

9. [Currently Amended] A method of claim 4 wherein the most narrowly defined grouping ~~groupings~~ on the tree of relationship comprises a moiety selected from the group consisting of: a specific genus, a specific species, a race, serotype, type or other grouping below the species level.

10. [Currently Amended] A method of claim 4 in which ~~the signature probes are constructed by the method of claim 1~~ extent to which each particular oligonucleotide or sequence of length N is characteristic of each node in the tree of genetic relationship is obtained by:

- A. Compiling a database of nucleic acid sequences from a substantially homologous RNA or DNA comprising sequences from all organisms or viruses that will be incorporated into the analysis;
- B. Calculating the occurrence frequency and distribution of substantially every oligoribonucleotide or oligodeoxyribonucleotide sequence of length N in the sequence data base;
- C. Calculating a signature quality function which measures the extent to which each particular oligoribonucleotide or oligodeoxyribonucleotide sequence of length N is characteristic of each node in the bifurcating node phylogenetic tree of genetic relationships.

11. [Cancelled]

12. [Cancelled]

13. [Cancelled]

14. Cancelled]

15. [Cancelled]

16. [Cancelled]

17. [Cancelled]

18. [Cancelled]

19. [Currently Amended] A method of Claim 4 in which the signature probes are of length 6 or larger and where the nucleic acid is selected from the group consisting of ribosomal RNA, genomic DNA, 10S RNA, RNase P RNA, guide RNA, telomerase RNA, snRNAs, scRNAs, and DNA isolated from the spacer region between ribosomal RNA genes or a fragment of the foregoing.

20. [Cancelled]

21 [New]A method of claim 4 wherein the hybridization step comprises a feature selected from the group consisting of locked nucleic acids, polymerase chain reaction, RT-PCR, peptide nucleic acids, array detection, and magnetic detection.

Claim 22 [Cancelled]

23 [New] A method of claim 10 in which the signature quality index,  $Q_s$ , is calculated by substantially the equation:

$$\begin{aligned} Q_s &= (NGM / NGT) \times (1 - (NM - NGM) / NM) \\ &= (NGM^2) / (NGT \times NM) \end{aligned}$$

in which NM is the number of probe-matched organisms in the entire tree, NGM is the number of probe-matched organisms in the group of interest, and NGT is the number of organisms in the group under consideration.

24 [New] A method of claim 4 in which the oligonucleotides or sequences of length N comprise genes.

26 [New] A method of Claim 4 in which a set of not more than 15 oligonucleotides or sequences are used to determine the genetic affinity of at least 18 organisms or viruses.

27 [New] A method of Claim 4 in which the failure to detect a particular oligonucleotide or sequence increases the confidence with which the genetic affinity of an organism or virus is determined.

28 [New] A method of Claim 4 in which the genetic affinity of an organism or virus is determined by an experiment in which at least half the oligonucleotides or sequences tested are not detected, and more than one oligonucleotide or sequence is detected.

29. [New] A method of Claim 10 in which the signature quality function is calculated by a single formula which includes both the presence of sequences in a particular group of organisms or viruses and their presence in other organisms not belonging to that group of organisms or viruses.

30. [New] A method of Claim 4 in which the signature probes used have values of Qs averaging less than 0.95 when calculated by substantially the equation:

$$\begin{aligned} Q_s &= (NGM / NGT) \times (1 - (NM - NGM) / NM) \\ &= (NGM^2) / (NGT \times NM) \end{aligned}$$

in which NM is the number of probe-matched organisms in the entire tree, N GM is the number of probe-matched organisms in the group of interest, and NGT is the number of organisms in the group under consideration.

31. [New] A method of Claim 4 in which the signature probes used have values of Qs averaging less than 0.85 when calculated by substantially the equation:

$$\begin{aligned} Q_s &= (NGM / NGT) \times (1 - (NM - N GM) / NM) \\ &= (NGM^2) / (NGT \times NM) \end{aligned}$$

in which NM is the number of probe-matched organisms in the entire tree, N GM is the number of probe-matched organisms in the group of interest, and NGT is the number of organisms in the group under consideration.

32. [New] A method of Claim 4 in which the genetic affinity of an organism or virus not represented in the database is determined.

33. [New] A method of Claim 22 in which the genetic affinity of an organism or virus not represented in the database is determined.

34 [New] The method of claim 20 in which the nucleic acid signature sequences are labeled or chemically modified in their backbone, their sugar, nucleoside base, or any combination thereof.

35 [New] A method of determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising the steps of:

- A) Detecting a signal generated as a result of the presence of a plurality of signature sequences or their complements in the nucleic acid.
- B) Comparing a database of the signature sequences found in the nucleic

acid to a database of signature sequences found in a plurality of organisms or viruses

C) Determining which Domain, Kingdom, Phylum, Subphylum, Class, Subclass, Order, Suborder, Family, Subfamily, Genus, Species, or Subspecies shares specific genetic affinity with the unknown organism or virus by considering the quality and number of signal generating signature sequences that are shared with members of each grouping.

36. [New] A method of determining the genetic affinity of organisms or viruses in a test sample comprising detecting the presence of a plurality of signature sequences.

37. [New] A method of determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising in combination the steps of:

[A] Identifying the statistical frequency with which any particular oligonucleotide or sequence of length N is a signature of any genetic grouping including Domain, Kingdom, Phylum, Subphylum, Class, Subclass, Order, Suborder, Family, Subfamily, Genus, Species, Tribe, Subspecies or Serotype;

[B] Deriving a set comprising a plurality of nucleic acid signature probes of varying signature quality from a database of signature sequences such that the genetic affinity of organisms or viruses from multiple genetic groupings are represented in a single set of signature probes;

[C] Determining which signature sequences of the set are present in the test sample by hybridizing the signature probes to the target nucleic acid under conditions where a detectable signal will be produced by signature probes that hybridize to the nucleic acid;

[D] Identifying signature probes which produce detectable signal.

[E] Determining the most terminal genetic grouping that produced detectable signal in order to determine the closest genetic relatives of the organism or virus in the test sample;

[F] Optionally verifying the identification by establishing that a plurality of signature sequences distinct to parent, grandparent, and other genetic groupings are also present in the test sample.

38. [New] A method of claim 37 in which signature sequences are generated from a target nucleic acid by enzymatic digestion with a nuclease and identified by mass spectrometry.

39. [New] A method of claim 37 in which the database of signature sequences comprises a library of gene sequences from which signature sequences are identified by computational means as needed.